REMARKS

Claim 20 remains in the application. Claim 20 is the only claim in independent form.

Claim 20 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Office Action holds that claim 20 recites "obtaining epitope bearing clones displaying reactivity to antibodies present in sera of patients with early stage cancer but not in sera of normal individuals" and "identifying all epitope bearing clones that are specific to early stage cancer as markers indicative of early stage cancer". The Office Action holds that as step one only obtains sera from normal individuals and patients with cancer (not any specific stage of cancer), it remains unclear as to what is indicative of early stage cancer. In response thereto, the fact that all epitopes are obtained from patients with cancer (independent of stage) with the method of the present invention allows for the detection of early stage cancer. In other words, it is the amount of epitopes that are obtained that allows one to detect early stage cancer. With previous detection methods, only a few epitopes are found, and therefore, it is unlikely that early stage cancer can be detected. Therefore, the epitopes found with the present invention are indicative of early stage cancer.

The Office Action further holds that it is unclear how a clone can be a marker, and holds that the epitope itself can be a marker. In response thereto, Applicants have amended claim 20 to reflect that the epitope is a marker.

Reconsideration of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claim 20 stands rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Office Action holds that no support has been provided for the limitation that a "clone" is a "marker". In

response thereto, Applicant has amended claim 20 as stated above to reflect that the epitopes are markers. Reconsideration of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claim 20 stands rejected under 35 U.S.C. §103(b) as being unpatentable over Sioud, et al. in view of WO 99/39210 to Miller, et al. The Office Action holds that Sioud, et al. teaches the analysis of the humoral response in patients with cancer; libraries from breast cancer cell lines were biopanned and positive clones were selected; using serum antibodies from patients with breast cancer, IgG-binding phage-encoded cDNA products were selected and the clones identified important antigens including p53, pentraxin and others; and the selected phage-displayed cDNA products were recognized by a significant number of breast cancer sera as compared to normal individuals. The Office Action holds that Sioud, et al. does not specifically teach a "microarray of markers within sera. However, Miller, et al. teaches a high-density protein array for proteome analysis and the Office Action holds that it would have been *prima facie* obvious to one skilled in the art to have utilized the techniques of Sioud to biopan and select clones to array in a large format as presented by Miller, et al.

Claim 20 also stands rejected under 35 U.S.C. §103(b) as being unpatentable over Sioud, et al. in view of U.S. Patent Application Publication No. 2003/0003516 to Robinson, et al. The Office Action holds that Sioud, et al. does not specifically teach a "microarray" of markers within sera. However, Robinson, et al. teaches an epitope array for determining a specificity profile in a patient and the array is high density. Therefore, the Office Action holds that it would have been *prima facie* obvious to one skilled in the art to have used the methods of Sioud with the high-density arrays of Robinson, et al.

More specifically, it is undisputed that the primary reference, the Sioud, et al., reference, discloses the step of biopanning libraries for selecting phage display cDNA products recognized by a significant number of breast cancer sera as compared to sera from normal individuals. The Sioud, et al., reference concluded that "the obtained results demonstrate that phage display could be a valuable method for the identification of antigens recognized by the

humoral immune system in patients with cancer." (Sioud, et al., reference, abstract).

As previously argued by Applicants, it is admitted that it is well-known to biopan for a specific composition, as disclosed in the Sioud, et al. reference. That is, the Sioud, et al., reference discloses biopanning methods aimed at determining the presence of a single significant marker. There is no disclosure in the Sioud, et al. reference of a method or assay that simultaneously screens for an unlimited number of markers within sera. The cited reference only teaches obtaining approximately five to ten markers. This is known in the art to be a low throughput method. This is consistent with the commonly accepted convention of determining a single marker for diagnostic purposes, such as those used for prostate cancer, breast cancer, or the like. Moreover, the methodology disclosed in the Sioud, et al., reference teaches away from the use of a large array, or more specifically, including all epitopes uncovered during biopanning related to a disease, because the primary goal, as disclosed in the first full paragraph of page 718 of the Sioud, et al., reference is to ". . . enrich for the best binders. If the selection is specific an increase in the number of positive clones is likely."

"[It is an] error to find obviousness where references 'diverge from and teach away from the invention at hand'". *In re Fine*, 5 USPQ2d 1596, 1599 (Fed. Cir. 1988) (citing *W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1550, 220 USPQ 303, 311 (Fed. Cir. 1983)).

The additional selections disclosed in the Sioud, et al., reference were designed to increase the specificity for finding a few highly specific markers. Identifying ***all*** epitopes in the present invention and therefore requiring a large protein array is certainly not the same as identifying ***five to ten*** markers as in Sioud, et al. Certainly, if five to ten markers are sufficient to detect cancer according to Sioud, et al., there is no reason to use a microarray to obtain markers.

"If, however, the examiner does produce a prima facie case, the burden of coming forward with evidence or arguments shifts to the applicant who may submit additional evidence of nonobviousness, such as comparative test data showing that the claimed invention possesses improved properties not expected by the prior art." MPEP 2142 (2100-127).

Applicants submit herein the Declaration of Dr. Michael Tainsky, an inventor of the present invention. The present invention provides unexpected results in view of the convention of the prior art. The present invention, as set forth in independent claim 20, is characterized by identifying ***all epitope-bearing clones*** that are specific to early-stage cancer and including ***all epitopes identified*** in protein arrays for detecting early-stage cancer. This teaching goes directly against the teachings of the cited prior art. Moreover, the present invention as set forth in pending claim 20 provides unexpected results by providing a broad range, yet sensitive assay, capable of detecting early-stage cancer, as supported on page 42 of the presently pending patent application. The present invention provides a method of identifying and detecting markers indicative of early-stage cancer, thereby allowing the practitioner to utilize more specific diagnostic procedures to confirm the early-stage cancer and then prescribe early-stage treatments. The cited prior art does not provide markers nor does it even suggest the provision of markers for such early-stage detection of cancer. Treatment of early-stage cancer is known to be significantly more effective than treatment of later-stage cancer. Choosing only a few markers in Sioud, et al. through low throughput approaches would be insensitive, i.e. many false negatives would be detected among cancer bearing test subjects. Hence, the present invention provides unexpected results not obtained by the prior art. That is, the present invention includes all epitopes identified in protein array assays for detecting early-stage cancer. Such unexpected results overcome a *prima facie* obviousness-type rejection as a matter of law. Hence, it is respectfully submitted that independent claim 20 is patentable over the cited prior art.

The remaining dependent claims not discussed above are ultimately dependent upon at least one of the independent claims discussed above. No

prior art reference makes up for the deficiencies of that reference as applied against the independent claims as no prior art reference discloses or suggests the invention as set forth in the claims as discussed in detail above.

In conclusion, it is respectfully submitted that the presently pending claims are in condition for allowance, which allowance is respectfully requested.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

KOHN & ASSOCIATES, PLLC

Kenneth I. Kohn, Reg. No. 30,955
Customer No. 48924

Dated: June 30, 2008

CERTIFICATE OF ELECTRONIC FILING VIA EFS-WEB

Date of Electronic Filing: June 30, 2008

I hereby certify that this correspondence is being electronically filed with the United States Patent & trademark Office on the above date.

Terry Horst